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10/527,370	11/28/2005	Atsushi Sogabe	18965-002US1 t97-183833C/	5590

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EXAMINER	
KIM, ALEXANDER D	
ART UNIT	**PAPER NUMBER**
1656	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,370	SOGABE ET AL.	
	Examiner	Art Unit	
	ALEXANDER D. KIM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2, 4 and 13-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 4 and 13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *ExPASy*.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (mailed on 09/20/2007), Applicants filed two responses and amendments received on 12/20/2007 and 12/21/2007, respectively. Said amendments cancelled Claims 1, 3 and 5-12; amended Claims 2 and 4; and added new Claims 13-16 from the previous claims filed on 3/10/2005.

Claims 2, 4 and 13-16 are pending in the instant Office action and will be examined herein.

Withdrawn-Objections to the Specification

2. The previous objection to the specification because the title is not descriptive of the claims is withdrawn by virtue of Applicants' amendment.

3. The previous objection to the specification because the Abstract does not completely describing the disclosed subject matter is withdrawn by virtue of Applicants' amendment.

New-Objections to the Specification

4. The abstract of the disclosure is objected to because the abstract must be provided on a separate page and have one paragraph. Correction is required. See MPEP § 608.01(b).

Withdrawn-Claim Rejections - 35 USC § 112

5. The previous rejection of Claim 1 under 35 U.S.C. 112, second paragraph, for reciting the limitation “high resistance against preservative” is withdrawn by virtue of cancelling Claim 1.

6. The previous rejection of Claim 2 (Claim 3 dependent therefrom) under 35 U.S.C. 112, second paragraph, for reciting the limitation “remaining activity ratio is 70% or more” is withdrawn by virtue of Applicants' amendment.

New-Claim Rejections - 35 USC § 112

7. Claims 2-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These rejections are necessitated by the amendment.

(a) Claims 2 (Claim 4 dependent therefrom) recites the limitation "at lest 90% or more of the activity" and "at least 70% or more of the kinase activity", which are relative term. The % activity can be varied depending on assay condition (e.g., different pH) for the glycerol kinase activity. Thus, any residual activity by the claimed protein can be calculated to have at least 70% or 90% using very low activity by the same protein (that

is measured at sub-optimal assay condition, for example) as a point of reference. Appropriate clarification is required.

(b) Claims 14 and 15 recite the limitation "at least 70% or more of the glycerol kinase activity" and "at least 92% or more of the kinase activity", which are relative term. The % activity can be varied depending on assay condition (e.g., different pH) for the glycerol kinase activity. Thus, any residual activity by the claimed protein can be calculated to have at least 70% or 90% using very low activity by the same protein (that is measured at sub-optimal assay condition, for example) as a point of reference. Appropriate clarification is required.

Claim Rejections - 35 USC § 112

8. Claims 2, 4 and 13-15 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous Claims 1-4. In response to this rejection, applicants have cancelled Claims 1, 3 and 5-12; amended Claims 2 and 4; and added new Claims 13-15 and traverse the rejection as it applies to the newly amended claims and added claims. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue that "the skilled artisan would have concluded that the inventors were in possession (at the time of filing of the present application) of the necessary common attributes possessed by the members of the claimed genus" (see top of page 10, Remarks received on 12/20/2007). Applicants also argue that the claimed genus of isolated proteins embraced by the claims does not have substantial variation, since all of the proteins must have glycerol kinase activity and more, such as the specified molecular weight; thus, the claim is not directed to a mere desired result without structure as was the case in Lilly (see top of page 10, Remarks received on 12/20/2007). Applicants further argue the claim 4 specifies the structure of the protein consisting of an amino acid sequence represented by SEQ ID NO: 1.

However, as applicants acknowledged by recitation of the MPEP, the Examiner acknowledge that the written description of claimed genus may be satisfied through a sufficient description of a representative number of species by disclosing a relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, as long as said structure and/or properties is "coupled with known or disclosed correlation between function and structure" (see bottom of page 8, Remarks filed on 12/20/2007, it is noted that applicants have recited "correction" in place of the term "correlation"). The recitation of "about 55,000 daltons" (wherein the term about is a broad term encompassing any protein having other size) is the only structure of claimed protein without the correlation to any functional characteristic recited in Claim 1. The numerous chemical properties described in Claim 1 cannot satisfy the written description and useless for sufficient written description requirement without the correlation between

said structure and said function by the instant disclosure. Thus, one skilled in the art would not be able to possess the full scope of the claimed isolated protein with function, e.g., glycerol kinase activity that has ability to modify glycerol, in the presence of ATP, to glycerol-3-phosphoric acid. Furthermore, the Claim 4 is not limited to a isolated protein of SEQ ID NO: 1. As written, "a protein consisting of an amino acid sequence represented by SEQ ID NO: 1" encompass any protein or variant as long as it contain any amino acid sequence of SEQ ID NO: 1 as small as two consecutive amino acids from SEQ ID NO: 1. Also, Claims 13-15 are not limited to a protein of SEQ ID NO: 1 but includes any variations of SEQ ID NO: 1. Moreover, the instant application failed to describe the correlation between the structural variant of SEQ ID NO: 1 (as encompassed by the and function recited in Claim 1) and the function of any glycerol kinase activity. For the reasons above, the instant specification and the prior art cannot describe the structure of a very broad claimed genus and one skilled in the art would not be in possession of the claimed genus of glycerol kinase by the instant specification.

9. Claims 2, 4 and 13-15 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for glycerol kinase consisting of SEQ ID NO: 1 from *Cellulomonas sp.* JCM2471, does not reasonably provide enablement for any isolated glycerol kinase or variants of SEQ ID NO: 1 and/or having chemical properties as recited in Claims 2, 4 and 13-15.

The specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use of the invention commensurate

in scope with these claims.

The rejection was stated in the previous office action as it applied to previous Claims 1-4. In response to this rejection, applicants have cancelled Claims 1, 3 and 5-12; amended Claims 2 and 4; and added new Claims 13-15 and traverse the rejection as it applies to the newly amended claims and added claims. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue that the instant claims are enabled for one skilled in the art to make and use the claimed isolated proteins with little more than routine experimentation because the instant application disclose the protein of SEQ ID NO: 1; tested extensively and found to have a number of chemical and physical properties as shown in Examples 1-6; and the standard mutagenesis techniques can be used produce variants of SEQ ID NO: 1.

The Examiner acknowledge the SEQ ID NO: 1 and the making a variants using standard mutagenesis technique is routine. However, applicants disclose no direction or guidance on how to make and use any other glycerol kinase with recited glycerol kinase activity as recited in Claims. Because the lack of direction or guidance on how to make and use the full scope of the claimed protein encompassing any variation of SEQ ID NO: 1 with the recited function of glycerol kinase activity, the undue experimentation is necessary for one skilled on the art. As applicants acknowledged, the recited chemical properties recited in claims are the properties of SEQ ID NO: 1 (see page 11 lines 14-15, remarks filed on 12/20/2007) and without the direction or guidance of how to vary the SEQ ID NO: 1 so that the protein would have or maintain the full scope of

the properties encompassed by Claims require undue experimentation for one skilled in the art.

One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. The specification does not support the broad scope of the claims which encompass all modifications and fragments because the specification does not disclose the following : (A) the general tolerance to modification and extent of such tolerance; (B) specific positions and regions throughout the protein's sequence which can be predictably modified and which regions are critical for biological activity; (C) what fragments, if any, can be made which have the desired glycerol kinase activity of the intact protein; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid substitutions or modifications and/or fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made in a (Name of protein) structure yielding similar folding and activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Withdrawn-Claim Rejections - 35 USC § 101

10. The previous rejection of Claims 2 and 4 under 35 U.S.C. §101 because the claimed invention is directed to non-statutory subject matter is withdrawn by virtue of Applicants' amendment.

Claim Rejections - 35 USC § 102

11. Claims 2, 4 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by reference by Wilkison et al. (1991, The Journal of Biological Chemistry, vol. 266, pages 16886-16891).

The rejection was stated in the previous office action as it applied to previous Claims 1-4. In response to this rejection, applicants have cancelled Claims 1, 3 and 5-12; amended Claims 2 and 4; and added new Claims 13-16 and traverse the rejection as it applies to the newly amended claims and added claims. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue that the instant rejection is based on the inherent characteristic based on the fact that a certain result or characteristic may occur or be present in the prior art, which is not sufficient not establish the inherency of that result or characteristic. Applicants further argue that the Wilkison et al. do not even disclose or even suggest that the glycerol kinase exhibited any of the chemical or physical properties in Claim 2, e.g., glycerol kinase of Wilkison et al. which was not tested for

forming glycerol-3-phosphoric acid from the glycerol with ATP, and said glycerol kinase of Wilkison et al. do not disclose that the kinase consist of the SEQ ID NO: 1.

However, the instant rejection is based on the factual product that really exist and not "based on the fact that --- may occur". As noted previously, the glycerol kinase of Wilkison et al. was prepared from the same bacterial source for the glycerol kinase of SEQ ID NO: 1. Wilkison et al. teach the glycerol kinase having EC 2.7.1.30 (see top of right column, page 16887) wherein the kinase has activity to form glycerol-3-phosphate as evidenced by ExPASy (see attachment). Wilkison et al. also teach that [^{14}C]glycerol was formed from "[^{14}C]glycerol-P" (i.e., [^{14}C]glycerol 3-phosphate synthesized as disclosed in the Material section, on page 16886) as recited on page 16887, bottom left column; thus, teaching a formation of glycerol-3-phosphate from glycerol and phosphate donor such as ATP because the glycerol kinase of Wilkison et al. has reversible activity as evidenced by ExPASy (see attachment). Since the Office does not have the facilities for examining and comparing applicants' protein (and its source of microorganism *Cellulomonas sp*. JM2471) with the protein of Wilkison et al. (and its source *Cellulomonas sp.*), the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., the amino acid sequence of protein and/or the gene sequence of *Cellulomonas sp*. encoding said enzyme of the prior art, for example) does not possess the same material structural and functional characteristics of the claimed protein. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594. Even if the amino acid sequence of Wilkison et al. is not same as the instant SEQ ID NO: 1, the glycerol

kinase of Wilkison et al. meets the limitation of Claims 2, 4, and 13-15 because the Claims 2, 4, and 13-15 encompass any variant of SEQ ID NO: 1 as long as it has glycerol kinase activity with or without any derivatives of N-methylisothiazolone, which including any chemical.

Conclusion

12. Claims 2, 4, and 13-16 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered section in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEXANDER D. KIM whose telephone number is (571)272-5266. The examiner can normally be reached on 11AM-7:30PM.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/
Examiner, Art Unit 1656

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652